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## Following the successful development of Fuzeon Roche and Trimeris sign new research agreement to develop next generation HIV fusion inhibitors

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Roche and Trimeris today announced that they have signed a further research agreement to discover, develop and commercialise the next generation of HIV fusion inhibitors. This agreement affirms Roche and Trimeris' commitment to developing the next generation of fusion inhibitors to meet the future needs of HIV-infected patients.

The joint research agreement announced today expands upon a successful worldwide partnership that has been in place since 1999 which has already brought Fuzeon (enfuvirtide), the world's first fusion inhibitor to market. Fuzeon is the pioneer of the fusion inhibitor class and the first innovation in HIV treatment since 1996. Pre-treated patients using Fuzeon have been shown to be twice as likely to achieve undetectable levels of HIV in their blood, and long term data has demonstrated that the benefit of regimens containing Fuzeon lasted three times longer than those without. Longer term benefits are achieved with Fuzeon in patients who are less treatment experienced.

The research agreement will focus on the investigation of improved formulation and delivery technologies to enable less frequent administration of peptide fusion inhibitors and the discovery of new peptides with enhanced efficacy and resistance profiles. Due to challenges with achieving the technical profile required of the current formulation of an investigational compound called T-1249, Roche and Trimeris have decided to put the early stage clinical programme of T-1249 on hold.

"We are fully committed to Fuzeon, the first HIV fusion inhibitor which is now readily available for pre-treated HIV patients, and to developing the next generation of fusion inhibitors as follow on compounds, as rapidly and as rigorously as possible," said Dr David Reddy, Roche HIV Franchise Leader.

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"Trimeris is excited about expanding the research agreement with Roche which widens the prospects of developing future generations of improved peptide fusion inhibitors for patients with HIV" said Dr Dani Bolognesi, co-founder and CEO, Trimeris. "The research agreement Roche and Trimeris are announcing today also provides the opportunity to pursue improved formulations and delivery technologies which may be applicable to Fuzeon, T-1249 and future peptide fusion inhibitors."

#### Notes to Editors:

##### Safety of Fuzeon

Fuzeon is administered as a twice-daily subcutaneous injection. Local injection site reactions were the most frequent adverse events associated with the use of Fuzeon. In the TORO studies, 98 percent of patients had at least one local injection site reaction over the course of 48 weeks. In this treatment-experienced patient population, 4 percent of patients at 48 weeks discontinued treatment with Fuzeon as a result of injection site reactions.

An increased rate of some bacterial infections, primarily pneumonia, was seen in patients treated with Fuzeon. It is unclear if this increased incidence is related to Fuzeon use. The addition of Fuzeon to background antiretroviral therapy generally did not increase the frequency or the severity of the majority of adverse reactions. The majority of adverse reactions were of mild or moderate intensity.

Hypersensitivity reactions have occasionally been associated with Fuzeon therapy and in rare cases have recurred on re-challenge.

##### Fuzeon indication in the European Union

The indication for Fuzeon in the European Union is for "use in combination with other antiretroviral medicinal products for the treatment of HIV-1 infected patients who have received treatment with and failed on regimens containing at least one medicinal product from each of the following antiretroviral classes, protease inhibitors, non-nucleoside reverse transcriptase inhibitors and nucleoside reverse transcriptase inhibitors, or who have intolerance to previous antiretroviral regimens. In deciding on a new regimen for patients who have failed an antiretroviral regimen, careful consideration should be given to the treatment history of the individual patient and the patterns of mutations associated with different medicinal products. Where available, resistance testing may be appropriate."

##### Resistance to HIV drugs

It is estimated that in a single untreated person the virus can mutate to form around a billion new and potentially different versions of HIV every day. The incidence of drug resistant HIV among already treated patients is increasing at a disturbing rate. It was recently reported in one study that up to 50 percent of patients in North America are infected with a strain of the virus that has developed resistance

to one or more anti-HIV drug.

#### **Roche in HIV**

Roche is at the forefront of efforts to combat HIV infection and AIDS, committed since 1986 to groundbreaking research and development of innovative new drugs and diagnostic technology. Saquinavir was the first Protease Inhibitor (PI) and was first introduced by Roche in 1995 in the US.

As a consequence of Roche's continuous research and development, the combination of boosted saquinavir with zidovudine (1000/100 mg twice daily) has shown encouraging results in the MaxCmin 1 trial with high efficacy and an excellent safety and tolerability profile. Saquinavir/r was approved in the EU in August 2002. Viracept (nelfinavir), a leading PI is supplied by Roche outside the US and Canada. In first-line HIV therapy, Viracept delivers consistent long-term efficacy and safety. When used first line, Viracept also allows the subsequent use of both NNRTIs and other PIs for most patients due to its unique resistance pattern. Fuzeon received approval from the US Food and Drug Administration (FDA) in March 2003, and from the European Commission and Switzerland in May 2003 and Canada in July 2003. T-1249 is being co-developed by Roche and Trimeris.

The viral load measurements in the clinical trials for Fuzeon were performed using the AMPLICOR HIV-1 MONITOR TEST, version 1.5. This test from Roche Diagnostics is considered to be a highly sensitive measurement of the amount of HIV circulating in a patient's blood ("viral load"). With a limited number of treatment regimens available, the accurate monitoring of viral load levels is essential to establish and monitor the effectiveness of therapeutic regimens and assess the potential onset of drug resistance.

Roche is a committed partner of the Accelerating Access Initiative to increase access to HIV care in sub-Saharan Africa and the world's Least Developed Countries. For more information on Roche policy and pricing of HIV protease inhibitors for these regions and research in HIV, visit [www.roche-hiv.com](http://www.roche-hiv.com).

#### **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading innovation-driven healthcare groups. Its core businesses are pharmaceuticals and diagnostics. Roche is number one in the global diagnostics market and is the leading supplier of pharmaceuticals for cancer and a leader in virology and transplantation. As a supplier of products and services for the prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche employs roughly 65,000 people in 150 countries. The Group has alliances and research and development agreements with numerous partners, including majority ownership interests in Genentech

and Chugai.

#### **Roche Business Development and Alliance Strategy**

Roche's innovation strategy is based on strong in-house research with centers in Japan, Europe and the USA, and strategic alliances with Genentech and Chugai. Complementing and strengthening the Group's dynamic R&D capabilities are over 80 scientific and commercial collaborations with biotech companies and universities in clearly defined focus areas. In the past 18 months, Roche has formed over 55 new partnerships, which span a wide range of therapeutic areas and technologies, making it an industry leader. A key element of this strategy is to enable its partners to achieve their vision while maintaining their cultural identity and entrepreneurial spirit. An integral marker of the success of this innovation strategy is the growth and expansion of existing partnerships, such as this one between Roche and Trimeris.

#### **About Trimeris**

Trimeris, Inc. is a biopharmaceutical company engaged in the discovery, development and commercialization of novel therapeutic agents for the treatment of viral disease. The core technology platform of fusion inhibition is based on blocking viral entry into host cells. Fuzeon, approved in the U.S. and the European Union, is the first in a new class of anti-HIV drugs called fusion inhibitors. Trimeris is developing Fuzeon and future generations of peptide fusion inhibitors in collaboration with F. Hoffmann-La Roche Ltd. For more information about Trimeris, please visit the company's website at [www.trimeris.com](http://www.trimeris.com).

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#### **Further information:**

- [www.roche-hiv.com](http://www.roche-hiv.com)
- [www.health-kiosk.ch](http://www.health-kiosk.ch)

#### **Trimeris Safe Harbor Statement**

This document and any attachments may contain forward-looking information about the Company's financial results and business prospects that involve substantial risks and uncertainties. These statements can be identified by the fact that they use words such as "expect," "project," "anticipate," "intend," "plan," "believe" and other words and terms of similar meaning. Among the factors that could cause actual results to differ materially are the following: there is uncertainty regarding the success of research and development activities, regulatory authorisations and product commercialisations; the results of our previous clinical trials are not necessarily indicative of future clinical trials; and, our drug candidates are based upon novel technology, are difficult and expensive to manufacture and may cause unexpected side effects. For a detailed description of these factors, see Trimeris' Form 10-K filed with the Securities and Exchange Commission on March 27, 2003 and its periodic reports filed with the SEC.



## Investor Update

January 07, 2004

**U.S. FDA approves INVIRASE boosted with Ritonavir for use in treatment of HIV/AIDS**  
**New dosing strategy offers potent option in combination with other anti-HIV drugs**

Roche today announced U.S. Food and Drug Administration (FDA) approval of its protease inhibitor INVIRASE (saquinavir mesylate 1000 mg) for use with ritonavir (100 mg) in combination regimens for the treatment of HIV infection. This new dosing strategy increases ("boosts") blood levels of saquinavir to enable twice-daily dosing and eliminates the inadequate drug levels associated with use of INVIRASE alone.

FDA approval of Roche's supplemental New Drug Application (sNDA) for INVIRASE was based on data which showed that INVIRASE 1000 mg with ritonavir 100 mg twice-daily provides similar to or greater levels of saquinavir over a 24-hour period than those achieved with another formulation of saquinavir, Fortovase, 1200 mg three times per day. Fortovase with ritonavir was studied in a heterogeneous population of 148 HIV-infected patients. Results showed that 91 of 148 subjects (61 percent) achieved and/or sustained an undetectable HIV RNA levels (<400 copies/mL) at the completion of 48 weeks of treatment. The efficacy of INVIRASE with ritonavir or Fortovase (with or without ritonavir coadministration) has not been compared against the efficacy of antiretroviral regimens currently considered standard of care.

"INVIRASE with ritonavir is an attractive option for the treatment of HIV because it is designed to provide consistently therapeutic levels of saquinavir with twice-daily dosing," said Dr. Frank Palella, Assistant Professor of Medicine, Feinberg School of Medicine, Northwestern University, Chicago. "With saquinavir, physicians and patients have the benefit of eight years of clinical experience on which to base treatment decisions. Today's news confirms that only low, 100 mg doses of ritonavir are needed to achieve effective levels of saquinavir when given with 1000 mg INVIRASE."

INVIRASE capsules do not require refrigeration and are smaller in size than Fortovase capsules. Roche is developing a 500 mg formulation of INVIRASE, designed to be used in the new boosted dosing regimen, that will cut daily pill count in half. A filing for the 500 mg formulation is projected for submission to the FDA for review in 2004.

It is important to note that INVIRASE and Fortovase are not bioequivalent and cannot be used interchangeably. INVIRASE may be used only if it is to be combined with ritonavir, which significantly inhibits saquinavir's metabolism and provides plasma saquinavir levels at least equal to those achieved with Fortovase. Fortovase is the recommended formulation when using saquinavir as the sole protease inhibitor in an antiviral regimen.

"The approval of INVIRASE for boosted dosing is another important step in Roche's ongoing efforts to define the optimal use of saquinavir, which was developed from our company's laboratories as the first protease inhibitor for HIV," said Kathy Presto, Vice President, U.S. HIV Franchise, Roche. "We have invested significantly in clinical trials and will continue our commitment through development of the INVIRASE 500 mg tablet formulation."

#### Dosing of Boosted INVIRASE

The FDA approved dosing for boosted INVIRASE is 1000 mg of INVIRASE (5 x 200 mg capsules) in combination with ritonavir 100 mg, twice a day. Ritonavir should be taken at the same time as INVIRASE. INVIRASE and ritonavir should be taken within 2 hours after a meal.

#### About Roche

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Ritonavir is manufactured by Abbott Laboratories.

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## Investor Update

January 09, 2004 7:31 AM

Roche announced today that the U.S. Food and Drug Administration (FDA) has approved pre-filled syringes of Pegasys (Peginterferon alfa-2a) for the treatment of chronic hepatitis C.

Pegasys, a pegylated alpha interferon, and Copegus (ribavirin, USP) were approved by the FDA in December 2002 for use in combination for the treatment of adults with chronic hepatitis C who have compensated liver disease and have not previously been treated with interferon alpha. Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis.

Pegasys is the most prescribed interferon therapy in the United States for the treatment of chronic hepatitis C\*. Roche expects Pegasys pre-filled syringes to be available in pharmacies by the end of the month. Pre-filled syringes will be packaged four per box. Pegasys is currently available in vials as a pre-mixed solution.

"Taking a medication by self-injection can be challenging for some people," said Dr. David Bernstein, Director of Hepatology, North Shore University Hospital. "Reducing the number of steps involved can make the process less intimidating for patients and reduce the risk of errors."

The introduction of pre-filled syringes is yet another way in which Roche is working to add value to the management of hepatitis C, including:

- developing approaches to reduce the duration of treatment with Pegasys and Copegus and the dose of Copegus therapy for certain patients
- introducing Copegus with a list price or wholesale acquisition cost that is 43 percent less per milligram than the other available brand of ribavirin
- backing Pegasys with the most extensive development program ever undertaken in hepatitis C
- formulating Pegasys as a pre-mixed solution requiring no reconstitution prior to self-injection

Hepatitis C is a blood-borne infectious disease of the liver and the leading cause of cirrhosis and liver cancer and the number one reason for liver transplants in the U.S. An estimated 2.7 million Americans are chronically infected with hepatitis C.

Pegasys is dosed at 180mcg as a subcutaneous injection taken once a week. Copegus is available as a 200mg tablet, and is administered orally two times a day as a split dose.

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\* IMS weekly TRx data (week 49-52: Dec '03)

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